

SEQUENCE LISTING

<110> Crooke, Stanley T.
 Lima, Walter
 Wu, Hongjiang

<120> Methods of Using Mammalian RNase H and Compositions Thereof

<130> ISPH-0520

<140> US/09/781,712

<141> 2001-02-12

<150> US 09/684,254

<151> 2000-10-06

<150> US 09/343,809

<151> 1999-06-30

<150> US 09/203,716

<151> 1998-12-02

<150> US 60/067,458

<151> 1997-12-04

<160> 39

<170> PatentIn version 3.0

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<212> PRT

<213> Homo sapiens

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Val Asp Glu Ala Gly Arg Gly Pro Val Leu Gly Pro Met Val Tyr Ala

Ile Cys Tyr Cys Pro Leu Pro Arg Leu Ala Asp Leu Glu Ala Leu Lys 50 55 60

Val Ala Asp Ser Lys Thr Leu Leu Glu Ser Glu Arg Glu Arg Leu Phe
65 70 75 80

Ala Lys Met Glu Asp Thr Asp Phe Val Gly Trp Ala Leu Asp Val Leu 85 90 95

Ser Pro Asn Leu Ile Ser Thr Ser Met Leu Gly Trp Val Lys Tyr Asn 100 105 110

Leu Asn Ser Leu Ser His Asp Thr Ala Thr Gly Leu Ile Gln Tyr Ala 115 120 125

Leu Asp Gln Gly Val Asn Val Thr Gln Val Phe Val Asp Thr Val Gly 130 135 140

Met Pro Glu Thr Tyr Gln Ala Arg Leu Gln Gln Ser Phe Pro Gly Ile 145 150 155 160

Glu Val Thr Val Lys Ala Lys Ala Asp Ala Leu Tyr Pro Val Val Ser 165 170 175

Ala Ala Ser Ile Cys Ala Lys Val Ala Arg Asp Gln Ala Val Lys Lys 180 185 190

Trp Gln Phe Val Glu Lys Leu Gln Asp Leu Asp Thr Asp Tyr Gly Ser 195 200 205

Gly Tyr Pro Asn Asp Pro Lys Thr Lys Ala Trp Leu Lys Glu His Val 210 215 220

Glu Pro Val Phe Gly Phe Pro Gln Phe Val Arg Phe Ser Trp Arg Thr 225 230 235 240

Ala Gln Thr Ile Leu Glu Lys Glu Ala Glu Asp Val Ile Trp Glu Asp 245 250 255

Ser Ala Ser Glu Asn Gln Glu Gly Leu Arg Lys Ile Thr Ser Tyr Phe 260 265 270

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<213> Mus sp.

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Ile Cys Tyr Cys Pro Leu Ser Arg Leu Ala Asp Leu Glu Ala Leu Lys 50 55 60

Val Ala Asp Ser Lys Thr Leu Thr Glu Asn Glu Arg Glu Arg Leu Phe 65 70 75 80

Ala Lys Met Glu Glu Asp Gly Asp Phe Val Gly Trp Ala Leu Asp Val . 85 90 95

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Thr Glu Arg Ser Lys Thr Trp Asn Asn Phe Gly Asn Gly Ile Pro Cys 20 25 30

Val Leu Gly Ile Asp Glu Ala Gly Arg Gly Pro Val Leu Gly Pro Met
35 40 45

Val Tyr Ala Ala Ile Ser Pro Leu Asp Gln Asn Val Glu Leu Lys 50 55 60

Asn Leu Gly Val Asp Asp Ser Lys Ala Leu Asn Ġlu Ala Lys Arg Glu 65 70 75 80

Glu Ile Phe Asn Lys Met Asn Glu Asp Glu Asp Ile Gln Gln Ile Ile 85 90 95

Ala Tyr Ala Leu Arg Cys Leu Ser Pro Glu Leu Ile Ser Cys Ser Met
100 105 110

Leu Lys Arg Gln Lys Tyr Ser Leu Asn Glu Val Ser His Glu Ala Ala 115 120 125

Ile Thr Leu Ile Arg Asp Ala Leu Ala Cys Asn Val Asn Val Glu 130 135 140

Ile Lys Val Asp Thr Val Gly Pro Lys Ala Thr Tyr Gln Ala Lys Leu 145 150 155 160 Glu Lys Leu Phe Pro Gly Ile Ser Ile Cys Val Thr Glu Lys Ala Asp 165 170 175

Ser Leu Phe Pro Ile Val Ser Ala Ala Ser Ile Ala Ala Lys Val Thr 180 185 190

Arg Asp Ser Arg Leu Arg Asn Trp Gln Phe Arg Glu Lys Asn Ile Lys 195 200 205

Val Pro Asp Ala Gly Tyr Gly Ser Gly Tyr Pro Gly Asp Pro Asn Thr 210 215 220

Lys Lys Phe Leu Gln Leu Ser Val Glu Pro Val Phe Gly Phe Cys Ser 225 230 235 240

Leu Val Arg Ser Ser Trp Lys Thr Ala Ser Thr Ile Val Glu Lys Arg 245 250 . 255

Cys Val Pro Gly Ser Trp Glu Asp Asp Glu Glu Glu Gly Lys Ser Gln 260 265 270

Ser Lys Arg Met Thr Ser Trp Met Val Pro Lys Asn Glu Thr Glu Val 275 280 285

Val Pro Lys Arg Asn Met Glu Ile Asn Leu Thr Lys Ile Val Ser Thr 290 295 300

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<213> Saccharomyces cerevisiae

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Pro Met Val Tyr Ala Val Ala Tyr Ser Thr Gln Lys Tyr Gln Asp Glu 50 60

Thr Ile Ile Pro Asn Tyr Glu Phe Asp Asp Ser Lys Lys Leu Thr Asp 65 70 75 80

Pro Ile Arg Arg Met Leu Phe Ser Lys Ile Tyr Gln Asp Asn Glu Glu 85 90 95

Leu Thr Gln Ile Gly Tyr Ala Thr Thr Cys Ile Thr Pro Leu Asp Ile

100 105 110

Ser Arg Gly Met Ser Lys Phe Pro Pro Thr Arg Asn Tyr Asn Leu Asn 115 120 125

Glu Gln Ala His Asp Val Thr Met Ala Leu Ile Asp Gly Val Ile Lys 130 . 135 140

Gln Asn Val Lys Leu Ser His Val Tyr Val Asp Thr Val Gly Pro Pro 145 150 155 160

Ala Ser Tyr Gln Lys Lys Leu Glu Gln Arg Phe Pro Gly Val Lys Phe 165 170 175

Thr Val Ala Lys Lys Ala Asp Ser Leu Tyr Cys Met Val Ser Val Ala 180 185 190

Ser Val Val Ala Lys Val Thr Arg Asp Ile Leu Val Glu Ser Leu Lys 195 200 205

Arg Asp Pro Asp Glu Ile Leu Gly Ser Gly Tyr Pro Ser Asp Pro Lys 210 215 220

Thr Val Ala Trp Leu Lys Arg Asn Gln Thr Ser Leu Met Gly Trp Pro 225 230 235 240

Ala Asn Met Val Arg Phe Ser Trp Gln Thr Cys Gln Thr Leu Leu Asp 245 250 255

Asp Ala Ser Lys Asn Ser Ile Pro Ile Lys Trp Glu Glu Gln Tyr Met 260 265 270

Asp Ser Arg Lys Asn Ala Ala Gln Lys Thr Lys Gln Leu Gln Leu Gln 275 280 285

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Ile Leu Asp Pro Ala Arg Pro Ile Ala Gly Leu Asn Asp Ser Lys Lys 35 40 45

Leu Ser Glu Lys Arg Arg Leu Ala Leu Tyr Glu Glu Ile Lys Glu Lys 50 55 60

Ala Leu Ser Trp Ser Leu Gly Arg Ala Glu Pro His Glu Ile Asp Glu 65 70 75 80

Leu Asn Ile Leu His Ala Thr Met Leu Ala Met Gln Arg Ala Val Ala 85 90 95

Gly Leu His Ile Ala Pro Glu Tyr Val Leu Ile Asp Gly Asn Arg Cys100 105 110

Pro Lys Leu Pro Met Pro Ala Met Ala Val Val Lys Gly Asp Ser Arg 115 120 125

Val Pro Glu Ile Ser Ala Ala Ser Ile Leu Ala Lys Val Thr Arg Asp 130 135 140

Ala Glu Met Ala Ala Leu Asp Ile Val Phe Pro Gln Tyr Gly Phe Ala 145 150 155 160

Gln His Lys Gly Tyr Pro Thr Ala Phe His Leu Glu Lys Leu Ala Glu 165 170 175

His Gly Ala Thr Glu His His Arg Arg Ser Phe Gly Pro Val Lys Arg 180 185 190

Ala Leu Gly Leu Ala Ser 195

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<213> Homo sapiens

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<302> Human Type 2 RNase H

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<310> US/09/203,726

<311> 1998-12-02

<312> 1999-12-14

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Gln Val Asp Arg Phe Pro Ala Ala Arg Phe Lys Lys Phe Ala Thr Glu 50 55 60

Asp Glu Ala Trp Ala Phe Val Arg Lys Ser Ala Ser Pro Glu Val Ser 65 70 75 80

Glu Gly His Glu Asn Gln His Gly Gln Glu Ser Glu Ala Lys Pro Gly
85 90 95

Lys Arg Leu Arg Glu Pro Leu Asp Gly Asp Gly His Glu Ser Ala Gln
100 105 110

Pro Tyr Ala Lys His Met Lys Pro Ser Val Glu Pro Ala Pro Pro Val 115 120 125

Ser Arg Asp Thr Phe Ser Tyr Met Gly Asp Phe Val Val Val Tyr Thr 130 135 140

Asp Gly Cys Cys Ser Ser Asn Gly Arg Arg Lys Pro Arg Ala Gly Ile 145 150 155 160

Gly Val Tyr Trp Gly Pro Gly His Pro Leu Asn Val Gly Ile Arg Leu 165 170 175

Pro Gly Arg Gln Thr Asn Gln Arg Ala Glu Ile His Ala Ala Cys Lys 180 185 190

Ala Ile Glu Gln Ala Lys Thr Gln Asn Ile Asn Lys Leu Val Leu Tyr 195 200 205

Thr Asp Ser Met Phe Thr Ile Asn Gly Ile Thr Asn Trp Val Gln Gly 210 215 220

Trp Lys Lys Asn Gly Trp Lys Thr Ser Ala Gly Lys Glu Val Ile Asn 225 230 235 240

Lys Glu Asp Phe Val Ala Leu Glu Arg Leu Thr Gln Gly Met Asp Ile 245 250 255

Gln Trp Met His Val Pro Gly His Ser Gly Phe Ile Gly Asn Glu Glu 260 265 270

Ala Asp Arg Leu Ala Arg Glu Gly Ala Lys Gln Ser Glu Asp 275 285

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<211> 286

<212> PRT

<213> Homo sapiens

<300>

<301> Wu et al.

<302> Molecular Cloning and Expression of cDNA for Human RNase H

<303> Antisense Nucleic Acid Drug Design

<304> 8

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<306> 53-61

<307> 1998-02-08

<308> AF039652

<309> 1998-04-02

<400> 7

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Arg Gly Arg Lys Thr Gly Val Phe Leu Thr Trp Asn Glu Cys Arg Ala 35 40 45

Gln Val Asp Arg Phe Pro Ala Ala Arg Phe Lys Lys Phe Ala Thr Glu 50 60

Asp Glu Ala Trp Ala Phe Val Arg Lys Ser Ala Ser Pro Glu Val Ser 65 70 75 80

Glu Gly His Glu Asn Gln His Gly Gln Glu Ser Glu Ala Lys Ala Ser 85 90 95

Lys Arg Leu Arg Glu Pro Leu Asp Gly Asp Gly His Glu Ser Ala Glu 100 105 110

Pro Tyr Ala Lys His Met Lys Pro Ser Val Glu Pro Ala Pro Pro Val 115 120 125

Ser Arg Asp Thr Phe Ser Tyr Met Gly Asp Phe Val Val Val Tyr Thr 130 135 140

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Gly Val Tyr Trp Gly Pro Gly His Pro Leu Asn Val Gly Ile Arg Leu 165 170 175

Pro Gly Arg Gln Thr Asn Gln Arg Ala Glu Ile His Ala Ala Cys Lys 180 185 190

Ala Ile Glu Gln Ala Lys Thr Gln Asn Ile Asn Lys Leu Val Leu Tyr 195 200 205

Thr Asp Ser Met Phe Thr Ile Asn Gly Ile Thr Asn Trp Val Gln Gly 210 215 220

Trp Lys Lys Asn Gly Trp Lys Thr Ser Ala Gly Lys Glu Val Ile Asn 225 230 235 240

Lys Glu Asp Phe Val Ala Leu Glu Arg Leu Thr Gln Gly Met Asp Ile 245 250 255

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Ala Asp Arg Leu Ala Arg Glu Gly Ala Lys Gln Ser Glu Asp 275 280 285

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<213> Homo sapiens

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<301> Cerritelli and Crouch

<302> Cloning, Expression and Mapping of Ribonucleases H of Human and Mouse Related to Bacterial RNase HI

<303> Genomics

<304> 53

<305> 3

<306> 300-307

<307> 1998-11-01

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Arg Gly Arg Lys Thr Gly Val Phe Leu Thr Trp Asn Glu Cys Arg Ala 35 40 45

Gln Val Asp Arg Phe Pro Ala Ala Arg Phe Lys Lys Phe Ala Thr Glu
50 60

Asp Glu Ala Trp Ala Phe Val Arg Lys Ser Ala Ser Pro Glu Val Ser 65 70 75 80

Glu Gly His Glu Asn Gln His Gly Gln Glu Ser Glu Ala Lys Ala Ser 85 90 95

Lys Arg Leu Arg Glu Pro Leu Asp Gly Asp Gly His Glu Ser Ala Glu 100 105 110 Pro Tyr Ala Lys His Met Lys Pro Ser Val Glu Pro Ala Pro Pro Val 115 120 125

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Ser Arg Asp Thr Phe Ser Tyr Met Gly Asp Phe Val Val Val Tyr Thr 130 135 140

Asp Gly Cys Cys Ser Ser Asn Gly Arg Arg Pro Arg Ala Gly Ile 145 150 155 160

Gly Val Tyr Trp Gly Pro Gly His Pro Leu Asn Val Gly Ile Arg Leu 165 170 175

Pro Gly Arg Gln Thr Asn Gln Arg Ala Glu Ile His Ala Ala Cys Lys 180 185 190

Ala Ile Glu Gln Ala Lys Thr Gln Asn Ile Asn Lys Leu Val Leu Tyr 195 200 205

Thr Asp Ser Met Phe Thr Ile Asn Gly Ile Thr Asn Trp Val Gln Gly 210 215 220

Trp Lys Lys Asn Gly Trp Lys Thr Ser Ala Gly Lys Glu Val Ile Asn 225 230 235 240

Lys Glu Asp Phe Val Ala Leu Glu Arg Leu Thr Gln Gly Met Asp Ile 245 250 255

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Ala Asp Arg Leu Ala Arg Glu Gly Ala Lys Gln Ser Glu Asp 275 280 285

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<211> 286

<212> PRT

<213> Homo sapiens

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<301> Frank, Braunshofer-Reiter, Poltl and Holzmann

<302> Cloning, Subcellular Localization and Functional Expression of Human RNase HII

<303> Biol. Chem.

<304> 379

<305> 99

<306> 1407-1412

<307> 1998-12-01

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Arg Gly Arg Lys Thr Gly Val Phe Leu Thr Trp Asn Glu Cys Arg Ala 35 40 45

Gln Val Asp Arg Phe Pro Ala Ala Arg Phe Lys Lys Phe Ala Thr Glu 50 55 60

Asp Glu Ala Trp Ala Phe Val Arg Lys Ser Ala Ser Pro Glu Val Ser 65 70 75 80

Glu Gly His Glu Asn Gln His Gly Arg Glu Ser Glu Ala Lys Ala Ser 85 90 95

Lys Arg Leu Arg Glu Pro Leu Asp Gly Asp Gly His Glu Ser Ala Glu
100 105 110

Pro Tyr Ala Lys His Met Lys Pro Ser Val Glu Pro Ala Pro Pro Val 115 120 125

Ser Arg Asp Thr Phe Ser Tyr Met Gly Asp Phe Val Val Val Tyr Thr 130 135 140

Asp Gly Cys Cys Ser Ser Asn Gly Arg Arg Arg Pro Arg Ala Gly Ile 145 150 155 160

Gly Val Tyr Trp Gly Pro Gly His Pro Leu Asn Val Gly Ile Arg Leu 165 170 175

Pro Gly Arg Gln Thr Asn Gln Arg Ala Glu Ile His Ala Ala Cys Lys 180 185 190

Ala Ile Glu Gln Ala Lys Thr Gln Asn Ile Asn Lys Leu Val Leu Tyr 195 200 205

Thr Asp Ser Met Phe Thr Ile Asn Gly Ile Thr Asn Trp Val Arg Gly 210 215 220

Trp Lys Lys Asn Gly Trp Lys Thr Ser Ala Gly Lys Glu Val Ile Asn 225 230 235 240

Lys Glu Asp Phe Val Ala Leu Glu Arg Leu Thr Gln Gly Met Asp Ile 245 250 255

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<301> Frank, Braunshofer-Reiter, Wintersberger, Grimm and Busen

<302> Cloning of the cDNA encoding the large subunit of human RNase HI, a homologue of the prokaryotic RNase HII

ATT INDICATED SHOULD

<303> Proc. Natl. Acad. Sci. USA

<304> 95

<305> 22

<306> 12872-12877

<307> 1998-10-27

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Ile Cys Tyr Cys Pro Leu Pro Arg Leu Ala Asp Leu Glu Ala Leu Lys 50 55 60

Val Ala Asp Ser Lys Thr Leu Leu Glu Ser Glu Arg Glu Arg Leu Phe 65 70 75 80

Ala Lys Met Glu Asp Thr Asp Phe Val Gly Trp Ala Leu Asp Val Leu 85 90 95

Ser Pro Asn Leu Ile Ser Thr Ser Met Leu Gly Arg Val Lys Tyr Asn 100 105 110

Leu Asn Ser Leu Ser His Asp Thr Ala Thr Gly Leu Ile Gln Tyr Ala 115 120, 125

Leu Asp Gln Gly Val Asn Val Thr Gln Val Phe Val Asp Thr Val Gly
130 140

Met Pro Glu Thr Tyr Gln Ala Gln Leu Gln Gln Ser Phe Pro Gly Ile 145 150 155 160

Glu Val Thr Val Lys Ala Lys Ala Asp Ala Leu Tyr Pro Val Val Ser 165 170 175

Ala Ala Ser Ile Cys Ala Lys Val Ala Arg Asp Gln Ala Val Lys Lys 180 185 190

Trp Gln Phe Val Glu Lys Leu Gln Asp Leu Asp Thr Asp Tyr Gly Ser

Gly Tyr Pro Asn Asp Pro Lys Thr Lys Ala Trp Leu Lys Glu His Val 210 215 220

Glu Pro Val Phe Gly Phe Pro Gln Phe Val Arg Phe Ser Trp Arg Thr 225 230 235 240

Ala Gln Thr Ile Leu Glu Lys Glu Ala Glu Asp Val Ile Trp Glu Asp 245 · 250 255

Ser Ala Ser Glu Asn Gln Glu Gly Leu Arg Lys Ile Thr Ser Tyr Phe 260 265 270

Leu Asn Glu Gly Ser Gln Ala Arg Pro Arg Ser Ser His Arg Tyr Phe 275 280 285

Leu Glu Arg Gly Leu Glu Ser Ala Thr Ser Leu 290 295

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<301> Cerritelli and Crouch

<302> Cloning, Expression and Mapping of Ribonucleases H of Human and Mouse Related to Bacterial RNase HI

<303> Genomics

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<307> 1998-11-01

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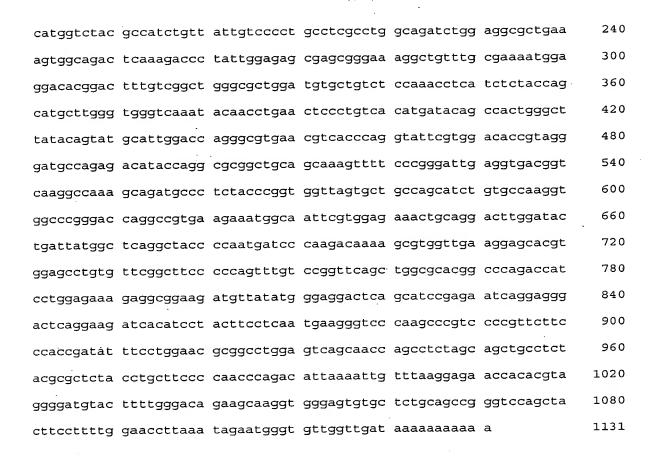
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Gln Val Asp Arg Phe Pro Ala Ala Arg Phe Lys Lys Phe Ala Thr Glu

| Asp 65 | Glu | Ala | Trp | Ala | Phe 70 | Val | Arg | ser | ser | 75 | ser | Pro | Asp | GIA | ser 80 |
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| Lys | Gly | Gln | Glu | Ser 85 | Ala | His | Glu | Gln | Lys 90 | Ser | Gln | Ala | Lys | Thr 95 | Ser |
| Lys | Arg | Pro | Arg 100 | Glu | Pro | Leu | Gly | Glu 105 | Gly | Glu | Glu | Leu | Pro 110 | Glu | Pro |
| Gly | Pro | Lys 115 | His | Thr | Arg | Gln | Asp 120 | Thr | Glu | Pro | Ala | Ala 125 | Val | Val | Ser |
| Lys | Asp 130 | Thr | Phe | Ser | Tyr | Met 135 | Gly | Glu | Ser | Val | Ile 140 | Val | Tyr | Thr | Asp |
| Gly 145 | Cys | Cys | Ser | Ser | Asn 150 | Gly | Arg | Lys | Arg | Ala 155 | Arg | Ala | Gly | Ile | Gly 160 |
| Val | Tyr | Trp | Gly | Pro 165 | Gly | His | Pro | Leu | Asn 170 | Val | Gly | Ile | Arg | Leu 175 | Pro |
| Gly | Arg | Gln | Thr 180 | Asn | Gln | Arg | Ala | Glu 185 | Ile | His | Ala | Ala | Cys 190 | Lys | Ala |
| Ile | Met | Gln 195 | Ala | Lys | Ala | Gln | Asn 200 | Ile | Ser | Lys | Leu | Val 205 | Leu | Tyr | Thr |
| Asp | Ser 210 | Met | Phe | Thr | Ile | Asn 215 | Gly | Ile | Thr | Asn | Trp 220 | Val | Gln | Gly | Trp |
| Lys 225 | Lys | Asn | Gly | Trp | Arg 230 | Thr | Ser | Thr | Gly | Lys 235 | | Val | Ile | Asn | Lys 240 |
| Glu | Asp | Phe | Met | Glu 245 | Leu | Asp | Glu | Leu | Thr 250 | Glņ | Gly | Met | Asp | Ile 255 | Gln |
| Trp | Met | His | Ile 260 | Pro- | Gly | His | Ser | Gly. 265 | Phe | Val | Gly | Asn | Glu 270 | Glu | Ala |
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| <213 | > : | Homo | sapi | ens | | | | | | | | | | | |

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| <223> | Antisense primer | |
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| <212> | DNA | |
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      26
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| 3 3 | | |
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| | | |
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| <400> cctctt | 32 tete caggatggte | 20 |
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| <212> | DNA | |
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| <220> | - | |
| <223> | Antisense oligonucleotide | |
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